Supporting Information Appendix

Participants in our sample were not formally characterized as free of psychiatric disease. However, in our sample, all subjects' BDI-II scores fell below the clinical cutoff level designated as indicating severe depression (a score of 29). Furthermore, when we restrict our analysis of the relationship between number of STPP G alleles and BDI-II to the subjects whose scores indicate "minimal" to "mild" depression (the 127 of our 141 subjects with scores of 0-19), the linear effect of STPP genotype remains significant (β = .271, p = .002). The STAI-T is not a clinical instrument as it does not assess impairment and thus no clinical cutoff levels exist. However, the STAI manual[20] reports norms for trait anxiety in a large sample of college age students and restricting our analysis to subjects who fall at or below the 90th percentile levels for each gender, the effect of STPP genotype on STAI-T scores remains significant (β = .261, p = .0038). These analyses suggest that the effect of STPP genotype upon anxiety and depressive symptoms reported in this manuscript is not driven by the inclusion of participants with undiagnosed clinical disorders.

Our bootstrapping mediation analyses were conducted using the publicly-available Multilevel Mediation and Moderation (M3) Toolbox[1,2]. Bootstrap estimates of the path coefficients were derived by randomly sampling with replacement 10,000 observations from our sample. The bootstrap mediation test implemented within the M3 toolbox uses a method known as the bias-corrected and accelerated (BCa) bootstrap[3], which estimates and adjusts for both bias and skewness in the bootstrap distribution, enabling the computation of an adjusted *z*-statistic based on the bootstrap confidence intervals, from which two-tailed p-values for each path coefficient were derived.

Tables

	TT	**GT**	**GG**	**Total**
FULL SAMPLE	n = 34	n = 60	n = 47	n = 141
Sex	20M, 14F	18M, 42F	16M, 31F	54M, 87F
Mean Age (SD)	21.0 (3.3)	21.0 (3.4)	21.3 (3.9)	21.1 (3.5)
Caucasian	25	23	15	63
Asian	2	28	28	58
Black/African-American	2	1	0	3
Hispanic	3	0	3	6
Mixed Race	2	8	1	11
FEAR CONDITIONING SUBSET	n = 28	n = 47	n = 35	n = 110
Mean Shock Level (SD)	37.4v (9.5)	36.6v (8.1)	36.6v (6.3)	36.8v (7.9)
Sex	15M, 13F	14M, 33F	13M, 22F	42M, 68F
Mean Age (SD)	20.6 (2.7)	21.0 (3.3)	21.6 (4.2)	21.1 (3.5)
Caucasian	21	22	11	54
Asian	2	19	22	43
Black/African-American	2	1	0	3
Hispanic	1	0	2	3
Mixed Race	2	5	0	7

Table S1: Participant demographics by STPP genotype group. Demographic information and experimental variables of participants in each STPP genotype group.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	-.589	.236		-2.495	.014
	Gender	-.022	.063	-.031	-.341	.734
	Age	.003	.009	.027	.294	.770
	Shock Level	.139	.039	.327	3.568	.001
	STPP G allele count	.087	.041	.197	2.151	.034

a. Dependent Variable: Spontaneous Recovery

Table S2: STPP association with spontaneous recovery was not related to age or gender of participants. Including all 110 subjects from the physiological analysis in a multiple regression with number of STPP G alleles, gender, age, and shock level as independent variables reveals that number of STPP G alleles remains a significant predictor of level of spontaneous recovery. Shock level is also a significant predictor of spontaneous recovery, however this effect is independent of the genotype effect.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	-.520	.244		-2.132	.036
	Race	-.019	.072	-.029	-.270	.788
	Gender	.012	.068	.018	.183	.855
	Age	.000	.009	-.003	-.032	.974
	Shock Level	.133	.040	.330	3.328	.001
	STPP G allele count	.091	.048	.207	1.869	.065

a. Dependent Variable: Spontaneous Recovery

Table S3: STPP association with spontaneous recovery was not related to race of participants. When we restrict analysis of the relationship between the STPP G allele and spontaneous recovery to the 97 Asian and Caucasian subjects in order to also include race (dummy-coded as 0 or 1)), gender (dummy-coded as 0 or 1), and age as regressors, the p value for the genotype effect is .065 due to reduced power in the smaller sample. However, there is no effect of race on spontaneous recovery.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	38.013	5.889		6.455	.000
	Race	.576	2.120	.026	.272	.786
	Gender	-1.330	2.043	-.059	-.651	.516
	Age	-.167	.267	-.055	-.626	.532
	STPP G allele count	5.095	1.431	.346	3.560	.001

a. Dependent Variable: STAI-T

Table S4: STPP association with trait anxiety was not related to race, gender, or age of participants. Including the 121 subjects who self-identify as Caucasian or Asian in a multiple regression analysis with number of STPP G alleles, gender (dummy-coded as 0 or 1), race (dummy-coded as 0 or 1), and age as independent variables, only number of G alleles was significantly related to STAI-T scores.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	13.076	3.919		3.337	.001
	Race	-.307	1.410	-.021	-.218	.828
	Gender	-.796	1.359	-.053	-.586	.559
	Age	-.333	.178	-.165	-1.871	.064
	STPP G allele count	2.857	.952	.292	3.000	.003

a. Dependent Variable: BDI-II

Table S5: STPP association with depressive symptoms was not related to race, gender, or age of participants. Including the 121 subjects who self-identify as Caucasian or Asian in a multiple regression analysis with number of STPP G alleles, gender (dummy-coded as 0 or 1), race (dummy-coded as 0 or 1), and age as independent variables, only number of G alleles was significantly related to BDI-II scores.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	-.560	.249		-2.246	.027
	Race	.013	.068	.020	.198	.844
	Gender	-.012	.068	-.018	-.180	.857
	Age	.001	.009	.013	.133	.894
	Shock Level	.137	.041	.341	3.381	.001
	5-HTTLPR S' allele count	.075	.047	.162	1.583	.117

a. Dependent Variable: Spontaneous Recovery

Table S6: 5-HTTLPR was not associated with spontaneous recovery even when controlling for race, gender, age, and shock level of participants. Including the 97 Asian and Caucasian subjects in our physiological sample in a multiple regression analysis with number of 5-HTTLPR S' alleles, gender (dummy-coded as 0 or 1), race (dummy-coded as 0 or 1), age, and shock level as independent variables, only shock level was significantly related to spontaneous recovery.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	41.655	6.223		6.694	.000
	Race	-1.766	2.131	-.080	-.829	.409
	Gender	-2.762	2.112	-.122	-1.308	.193
	Age	-.062	.279	-.020	-.221	.826
	5-HTTLPR S' allele count	1.357	1.434	.089	.946	.346

a. Dependent Variable: STAI-T

Table S7: 5-HTTLPR was not significantly associated with trait anxiety after controlling for race, gender, and age of participants. Including the 121 Asian and Caucasian participants in a multiple regression analysis with number of 5-HTTLPR S' alleles, gender (dummy-coded as 0 or 1), race (dummy-coded as 0 or 1), and age as independent variables, none were significantly related to STAI-T scores.

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
	(Constant)	14.390	4.060		3.545	.001
	Race	-1.385	1.390	-.094	-.996	.321
	Gender	-1.655	1.378	-.110	-1.201	.232
	Age	-.279	.182	-.138	-1.537	.127
	5-HTTLPR S' allele count	1.368	.935	.136	1.462	.146

a. Dependent Variable: BDI-II

Table S8: 5-HTTLPR was not significantly associated with depressive symptoms after controlling for race, gender, and age of participants. Including the 121 Asian and Caucasian participants in a multiple regression analysis with number of 5-HTTLPR S' alleles, gender (dummy-coded as 0 or 1), race (dummy-coded as 0 or 1), and age as independent variables, none were significantly related to BDI-II scores.

Figures

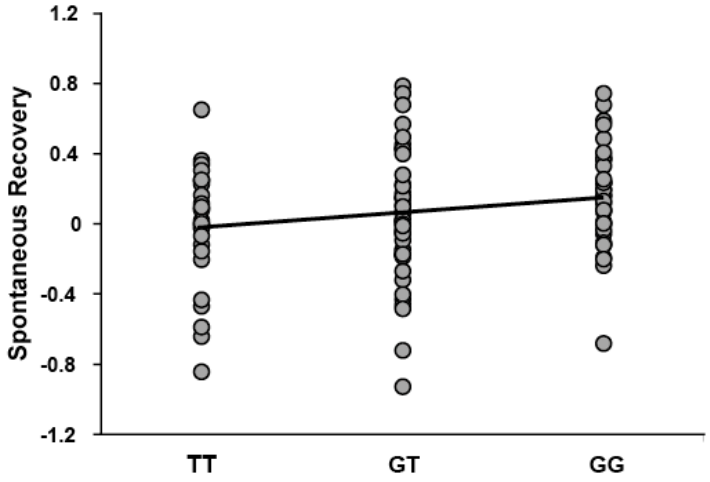

Figure S1: Scatterplot of association between STPP genotype and spontaneous recovery. Participants showed a significant linear increase in the spontaneous recovery of fear memory as a function of number of STPP G alleles (β =.191, p = .046).

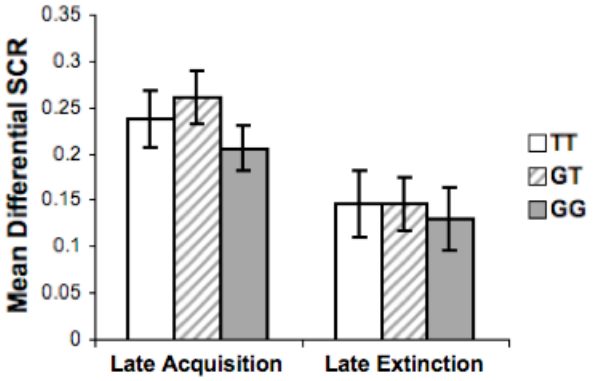

Figure S2: No differences in fear acquisition or extinction as a function of STPP genotype. Demonstrating the specificity of the STPP association with spontaneous recovery, there were no significant linear effects or pairwise group differences in conditioned fear responses during late fear acquisition (β = -.077, p = .422) or extinction (β = -.105, p = .266) as a function of STPP genotype.

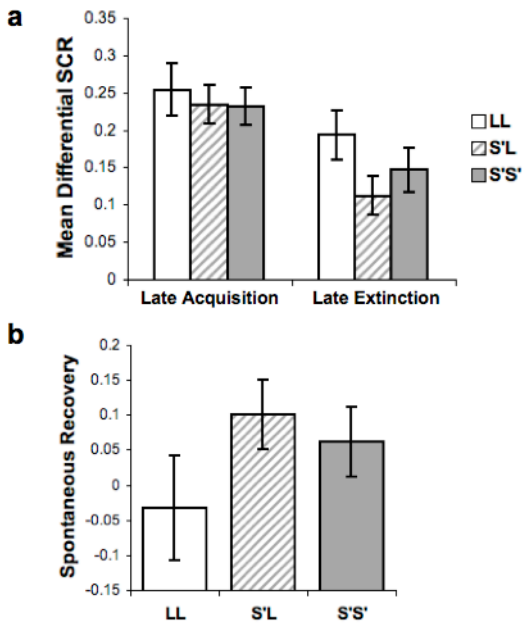

Figure S3: Variation in fear conditioning is not associated with 5-HTTLPR genotype. There were no significant linear effects or pairwise group differences in conditioned fear responses during (**a**) late fear acquisition (β = .041, p = .668), late extinction (β = -.086, p = .371), or (**b**) spontaneous recovery (β = .079, p = .410) as a function of 5-HTTLPR genotype.

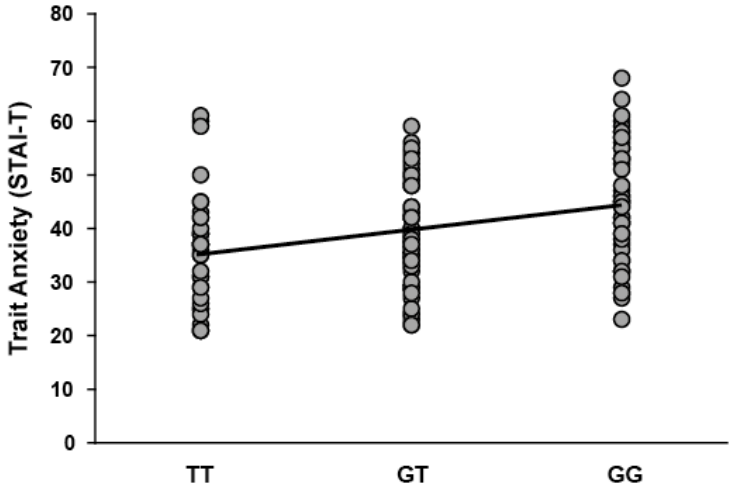

Figure S4: Scatterplot of association between STPP genotype and trait anxiety. Self-reported trait anxiety increased linearly as a function of number of STPP G alleles (STAI-T: β = .320, p = .00011).

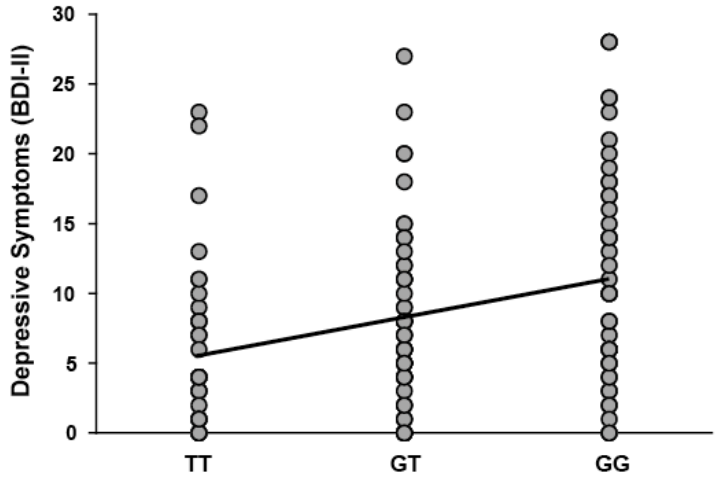

Figure S5: Scatterplot of association between STPP genotype and depressive symptoms. Depressive symptoms increased linearly as a function of number of STPP G alleles (BDI-II: β = .293, p = .0004).

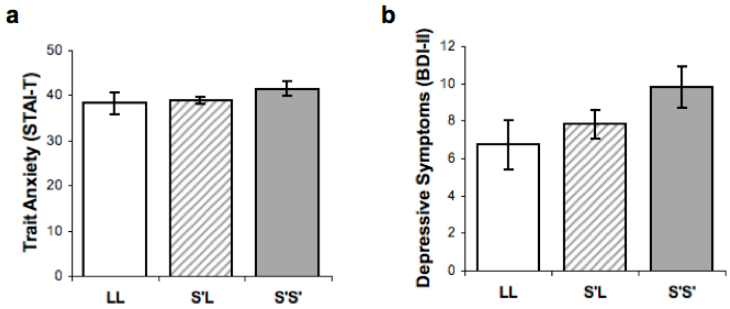

Figure S6: 5-HTTLPR shows a weak association with trait anxiety and depressive symptoms before accounting for the influence of correlation with the STPP. Simple linear regression shows a significant linear relationship between number of 5-HTTLPR S" alleles with (**a**) depressive symptoms (β = .170, p = .044) (**b**) and a trending association with trait anxiety (β = .121, p = .153).

References

1. Atlas LY, Bolger N, Lindquist MA, Wager TD (2010) Brain mediators of predictive cue effects on perceived pain. *J Neurosci* 30:12964-12977.

2. Davidson ML, Atlas LY, Lindquist MA, Bolger N, Wager TD (2008) The M3 Toolbox: the Multi-level Mediation/Moderation Framework for Connectivity Analyses in fMRI Data. (Poster presented at the annual meeting of the Cognitive Neuroscience Society, San Francisco, CA).

3. DiCiccio TJ, Efron B (1996) Bootstrap confidence intervals. *Statist Sci* 11(3):189-228.